Amendments to the Claims

The listing of claims below is intended to replace all prior listings of the claims:

1. (Original) A method of inducing tolerance to an antigen in a patient, the method comprising administering to the patient an agent which raises the effective cAMP concentration in a monocyte cell and granulocyte-macrophage colony stimulating factor (GMCSF) or a derivative thereof.

2. (Original) A method according to Claim 1 wherein the agent which raises the effective cAMP concentration in a monocyte cell is any one or more of a prostaglandin or agonist thereof, a ß-adrenergic agent, a blocker of cAMP export from the cell, forskolin or a derivative thereof, a cAMP phosphodiesterase inhibitor, a cAMP analogue, or cholera toxin or a derivative or fragment thereof.

3. (Original) A method according to Claim 2 wherein the blocker of cAMP export from the cell is probenicid or progesterone.

4. (Currently Amended) A ~~composition~~ method according to Claim 2 wherein the cAMP analogue is Sp-adenosine 3',5'-cyclic monophosphorothioate or 8-bromoadenosine 3',5' cyclic monophosphate or dibutryryl cAMP.

5. (Original) A method according to Claim 2 wherein the prostaglandin or agonist thereof stimulates cAMP production in a monocyte.

6. (Currently Amended) A method according to Claim 2 ~~or 5~~ wherein the prostaglandin or agonist thereof is any one of a prostaglandin E or an analogue thereof, ~~such as~~ prostaglandin E_2 or an analogue thereof, dinoprostone, gemeprost, misoprostol, alprostadil, limaprost, butaprost, 11-deoxy PGE1, AH23848, AH13205, or a 19-hydroxy PGE.

7. (Currently Amended) A method according to ~~any of Claims 1 to 6~~ Claim 1 wherein the GMCSF is human GMCSF having the amino acid sequence ~~as defined in Figure 1~~ of SEQ ID NO:2, or naturally occurring variants thereof.

8. (Currently Amended) A method according to ~~any of Claims 1 to 6~~ Claim 1 wherein the GMCSF is sargramostim.

9. (Currently Amended) A method according to ~~any of Claims 1 to 6~~ Claim 1 further comprising administering to the patient one or more of a monocyte chemotactic agent ~~to the patient~~ , a phosphodiesterase (PDE) inhibitor, and the antigen or a derivative thereof.

10. (Original) A method according to Claim 9 wherein the monocyte chemotactic agent is MCP-1 or MIP-1α.

11. (Canceled)

12. (Currently Amended) A method according to ~~Claim 11~~ Claim 9 wherein the PDE inhibitor is any one of 3-isobutyl-1-methylxanthine (IBMX), pentoxifylline (3,7-dihydro-3,7-dimethyl-1-(5-oxohexyl)-1H-purine-2,6-dione), rolipram (4-[3-cyclopentyloxy-4-methoxyphenyl]-2-pyrrolidinone), CP80 633, CP102 995, CP76 593, Ro-20-1724 (4-[3-butoxy-4-methoxybenzyl]-2-imidazolidinone), theophylline, or denbufylline (1,3-di-n-butyl-7-(2-oxopropyl)-xanthine).

13. (Currently Amended) A method according to ~~Claim 11 or 12~~ Claim 9 wherein the PDE inhibitor is selective for type IV PDE.

14. (Original) A method according to Claim 13 wherein the PDE inhibitor selective for type IV PDE is any one of rolipram (4-[3-cyclopentyloxy-4-methoxyphenyl]-2-pyrrolidinone), CP80 633, CP102 995, CP76 593, Ro-20-1724 (4-[3-butoxy-4-methoxybenzyl]-2-imidazolidinone), denbufylline (1,3-di-n-butyl-7-(2-oxopropyl)-xanthine), or CDP840, RP73401 or RS33793.

15. (Canceled)

16. (Currently Amended) A method according to ~~any one of Claims 1 to 15~~ Claim 9 wherein one or more of the agent which raises the effective cAMP concentration in a monocyte cell, the GMCSF or derivative thereof, the monocyte chemotactic agent, the PDE inhibitor, and the antigen or derivative thereof is administered (i) locally at a site where tolerance is required, (ii) systemically, (iii) orally, or (iv) as a suppository or capsule.

17-19. (Canceled)

20. (Currently Amended) A method according to ~~Claim 19~~ Claim 16 wherein the suppository or capsule has an enteric coating for release of the one or more of the agent which raises the effective cAMP concentration in a monocyte cell, the GMCSF or derivative thereof, the monocyte chemotactic agent, the PDE inhibitor, and the antigen or derivative thereof in the bowel of the patient.

21. (Currently Amended) A method according to ~~Claim 17~~ Claim 16 wherein at least the GMCSF or derivative thereof is administered subcutaneously or intravenously.

22. (Currently Amended) A method according to ~~any one of Claims 1 to 21~~ Claim 9 wherein any two or more of the agent which raises the effective cAMP concentration in a monocyte cell, the GMCSF or derivative thereof, the monocyte chemotactic agent, the PDE inhibitor, and the antigen or derivative thereof are administered simultaneously.

23. (Currently Amended) A method of ~~according to any one of Claims 1 to 22 for~~ combating a disease or condition associated with transplant rejection comprising:

performing the method according to Claim 1, wherein said administering is effective to combat a disease or condition associated with transplant rejection.

24. (Original) A method according to Claim 23 wherein the disease or condition associated with transplant rejection comprises graft versus host disease or host versus graft disease.

25. (Currently Amended) A method according to ~~Claim 23 or 24~~ Claim 23 wherein one or more of the agent which raises the effective cAMP concentration in a monocyte cell, the GMCSF or derivative thereof, ~~the~~ a monocyte chemotactic agent, ~~the~~ a PDE inhibitor, and the antigen or derivative thereof ~~is administered~~ is administered prior to the transplant.

26. (Currently Amended) A method according to ~~any one of Claims 23 to 25~~ Claim 23 wherein the antigen is HLA-A2.

27. (Currently Amended) A method of ~~according to any one of Claims 1 to 22 for~~ treating an autoimmune disease or condition comprising:

performing the method according to Claim 1, wherein said administering is effective to treat an autoimmune disease or condition.

28. (Currently Amended) A method according to Claim 27 wherein the autoimmune disease is selected from the group consisting of primary myxoedema, thyrotoxicosis, pernicious anaemia, autoimmune atrophic gastris, Addison's disease, insulin-dependent diabetes mellitus (IDDM), Goodpasture's syndrome, myasthenia gravis, sympathetic ophthalmia, multiple sclerosis (MS), autoimmune haemolytic anaemia, idiopathic leucopenia, ulcerative colitis, dermatomyositis, scleroderma, mixed connective tissue disease, rheumatoid arthritis, irritable bowel syndrome, systemic lupus erythromatosus (SLE), Hashimoto's disease, thyroiditis, Behcet's disease, coeliac disease/dermatitis herpetiformis, renal vasculitis, and demyelinating disease.

29. (Currently Amended) A method according to ~~Claim 27 or 28~~ Claim 27 wherein the antigen is a self-antigen.

30. (Currently Amended) A method according to ~~any one of Claims 27 to 29~~ Claim 27, wherein ~~if~~ the autoimmune disease is pernicious anaemia, and the antigen is vitamin B_{12}; ~~if~~ the disease is Addison's disease, and the antigen is adrenal antigen; ~~if~~ the disease is IDDM, and the antigen is glutamic acid decarboxylase (GAD), insulin, or IA-2; ~~if~~ the disease is Goodpasture's syndrome or renal vasculitis, and the antigen is renal antigen or endothelial antigen; ~~if~~ the disease is myasthenia gravis, and the antigen is the acetyl choline receptor; ~~if~~ the disease is sympathetic ophthalmia, and the antigen is ocular antigen; ~~if~~ the disease is multiple sclerosis (MS), and the antigen is myelin basic protein (MBP), proteolipid protein (PLP), or myelin oligodendrocyte glycoprotein (MOG); ~~if~~ the disease is autoimmune haemolytic anaemia, and the antigen is red cell antigen; ~~if~~ the disease is idiopathic leucopenia, and the antigen is leukocyte antigen; ~~if~~ the disease is ulcerative colitis, and the antigen is a food antigen or a viral antigen; ~~if~~ the disease is dermatomyositis, and the antigen is smooth muscle antigen; ~~if~~ the disease is scleroderma, and the antigen is a connective tissue antigen; ~~if~~ the disease is mixed connective tissue disease, and the antigen is a connective tissue antigen; ~~if~~ the disease is irritable bowel syndrome, and the antigen is a food antigen; ~~if~~

the disease is systemic lupus erythmatosus (SLE), and the antigen is a histone protein or immunoglobulin heavy chain; ~~if~~ the disease is Hashimoto's disease, primary myxoedema or thyrotoxicosis, and the antigen is thyroid antigen; ~~if~~ the disease is rheumatoid arthritis, and the antigen is type II collagen or a heat shock protein (HSP); ~~if~~ the disease is thyroiditis, and the antigen is thyroglobulin; ~~if~~ the disease is Behcet's disease, and the antigen is Sag, HLA-B44, B51, or HSP65; ~~if~~ the disease is Coeliac disease/Dermatitis herpetiformis, and the antigen is gliadin or the α fraction thereof; ~~and if~~ or the disease is demyelinating disease, and the antigen is myelin.

31. (Currently Amended) A method of ~~according to any one of Claims 1 to 22 for~~ treating an allergic disease or condition in ~~the~~ a patient comprising:

performing the method according to Claim 1, wherein said administering is effective to treat an allergic disease or condition in the patient.

32. (Original) A method according to Claim 31 wherein the allergic disease or condition is allergic asthma.

33. (Currently Amended) A method according to ~~Claim 31 or 32~~ Claim 31, wherein the antigen is a mite allergen, a dust allergen, a cat allergen, a dog allergen or a horse allergen.

34. (Currently Amended) A method according to ~~any one of Claims 1 to 33~~ Claim 1, wherein the induced tolerance to the antigen is effective to treat an aberrant or undesired immune or inflammatory response to the antigen in the patient.

35. (Original) A method according to Claim 34 wherein the aberrant or undesired immune or inflammatory response involves a deficiency in IL-10 production.

36. (Original) A composition comprising an agent which raises the effective cAMP concentration in a monocyte cell and granulocyte-macrophage colony stimulating factor (GMCSF) or a derivative thereof.

37. (Currently Amended) A composition according to Claim 36 wherein the agent which raises the effective cAMP concentration in a monocyte cell is any one or more of a prostaglandin or agonist thereof, a β-adrenergic agent, a blocker of cAMP export

from the cell, forskolin or a derivative thereof, a cAMP phosphodiesterase inhibitor, a cAMP analogue, or cholera toxin or a derivative or fragment thereof.

38. (Original) A composition according to Claim 37 wherein the blocker of cAMP export from the cell is probenicid or progesterone.

39. (Original) A composition according to Claim 37 wherein the cAMP analogue is Sp-adenosine 3′,5′-cyclic monophosphorothioate or 8-bromoadenosine 3′,5′ cyclic monophosphate.

40. (Original) A composition according to Claim 37 wherein the prostaglandin or agonist thereof stimulates cAMP production in a monocyte.

41. (Currently Amended) A composition according to Claim 37 ~~or 40~~ wherein the prostaglandin or agonist thereof is a prostaglandin E or an analogue thereof, ~~such as~~ prostaglandin E_2 or an analogue thereof, dinoprostone, gemeprost, misoprostol, alprostadil, limaprost, butaprost, 11-deoxy PGE1, AH23848, AH13205, or a 19-hydroxy PGE.

42. (Currently Amended) A composition according to ~~any of Claims 36 to 41~~ Claim 36 wherein the GMCSF is human GMCSF having the amino acid sequence ~~as defined in Figure 1~~ of SEQ ID NO:2, or naturally occurring variants thereof.

43. (Currently Amended) A composition according to ~~any of Claims 36 to 41~~ Claim 36 wherein the GMCSF is sargramostim.

44. (Currently Amended) A composition according to ~~any of Claims 36 to 43~~ Claim 36 further comprising one or more of a monocyte chemotactic agent, a phosphodiesterase (PDE) inhibitor, and an antigen or derivative thereof.

45. (Original) A composition according to Claim 44 wherein the monocyte chemotactic agent is MCP-1 or MIP-1α.

46. (Canceled)

47. (Currently Amended) A composition according to ~~Claim 46~~ Claim 44 wherein the PDE inhibitor is any one of 3-isobutyl-1-methylxanthine (IBMX), pentoxifylline (3,7-dihydro-3,7-dimethyl-1-(5-oxohexyl)-1H-purine-2,6-dione), rolipram (4-[3-cyclopentyloxy-4-methoxyphenyl]-2-pyrrolidinone), CP80 633, CP102 995, CP76 593, Ro-20-1724 (4-[3-butoxy-4-methoxybenzyl]-2-imidazolidinone), theophylline, or denbufylline (1,3-di-n-butyl-7-(2-oxopropyl)-xanthine).

48. (Currently Amended) A composition according to ~~Claim 46 or 47~~ Claim 44 wherein the PDE inhibitor is selective for type IV PDE.

49. (Original) A composition according to Claim 48 wherein the PDE inhibitor selective for type IV PDE is any one of rolipram (4-[3-cyclopentyloxy-4-methoxyphenyl]-2-pyrrolidinone), CP80 633, CP102 995, CP76 593, Ro-20-1724 (4-[3-butoxy-4-methoxybenzyl]-2-imidazolidinone), denbufylline (1,3-di-n-butyl-7-(2-oxopropyl)-xanthine), or CDP840, RP73401 or RS33793.

50. (Canceled)

51. (Currently Amended) A pharmaceutical composition comprising the composition according to ~~any one of Claims 36 to 50~~ Claim 36 and a pharmaceutically acceptable carrier, diluent or excipient.

52-65. (Canceled)

66. (Original) A therapeutic system for inducing tolerance to an antigen in a patient, the system comprising an agent which raises the effective cAMP concentration in a monocyte cell and GMCSF or a derivative thereof.

67. (Currently Amended) A therapeutic system according to Claim 66 further comprising one or more of the ~~an~~ antigen ~~to which it is desired to induce tolerance~~, a monocyte chemotactic agent, and a phosphodiesterase (PDE) inhibitor.

68. (Canceled)

69. (Currently Amended) A therapeutic system according to ~~any of Claims 66 to 68~~ Claim 67 wherein one or more of the agent which raises the effective cAMP concentration in a monocyte cell, the GMCSF or derivative thereof, the monocyte chemotactic agent, the PDE inhibitor, and the antigen or derivative thereof is in a preparation for (i) administration locally at a site where tolerance is required, (ii) systemic administration, (iii) oral administration, or (iv) administration as a suppository or capsule.

70-72. (Canceled)

73. (Currently Amended) A method of stimulating or enhancing granulysin expression in cells of ~~the~~ a macrophage/monocyte lineage comprising administering to the cells a therapeutic system according to claim 66 ~~an agent which raises the effective cAMP concentration in a monocyte cell and GMCSF or a derivative thereof.~~

74. (Currently Amended) A method of treating a viral infection in a patient comprising administering to the patient a therapeutic system according to claim 66 ~~an agent which raises the effective cAMP concentration in a monocyte cell and GMCSF or a derivative thereof.~~

75. (Original) A method according to Claim 74 wherein the viral infection is a herpes simplex virus infection or a human papilloma virus infection.

76-77. (Canceled)

78. (Currently Amended) A method of stimulating or enhancing IL-10 expression in, and secretion from, cells of ~~the~~ a macrophage/monocyte lineage comprising administering to the cells a therapeutic system according to claim 66 ~~an agent which raises the effective cAMP concentration in a monocyte cell and GMCSF or a derivative thereof.~~

79. (Currently Amended) A method of treating a tumour in a patient comprising administering to the patient a therapeutic system according to claim 66 ~~an agent which raises the effective cAMP concentration in a monocyte cell and GMCSF or a derivative thereof~~.

80-81. (Canceled)